

CLAIMS

What is claimed is:

- Sub B4
1. A catalytic antagonist of a target molecule, said antagonist comprising a targeting moiety that specifically binds to said target molecule said targeting moiety being attached to an enzyme that degrades said target molecule to reduce binding of the target molecule to its cognate ligand and to said targeting moiety thereby resulting in the release of said antagonist thereby allowing said antagonist to bind and degrade another target molecule.
 2. The antagonist of claim 1, wherein said targeting moiety is joined to said enzyme through the sulfur group on a cysteine.
 3. The antagonist of claim 2, wherein said cysteine is a cysteine that is substituted for a native amino acid other than cysteine in said enzyme.
 4. The antagonist of claim 3, wherein said cysteine is a cysteine that is substituted for a native amino acid other than cysteine in or near a subsite comprising a substrate binding site of said enzyme.
 5. The antagonist of claim 4, wherein said cysteine is a cysteine that is substituted for an amino acid forming a substrate binding site.
 6. The antagonist of claim 3, wherein said enzyme is an enzyme selected from the group consisting of a protease, an esterase, an amidase, a peptidase, a lactamase, a cellulase, an oxidase, an oxidoreductase, a reductase, a transferase, a hydrolase, an isomerase, a ligase, a lipase, a phospholipase, a phosphatase, a kinase, a sulfatase, a lysozyme, a glycosidase, a nuclease, an aldolase, a ketolase, a lyase, a cyclase, a reverse transcriptase, a hyaluronidase, an amylase, a cerebroside and a chitinase.
 7. The antagonist of claim 6, wherein said enzyme is a serine hydrolase.
 8. The antagonist of claim 5, wherein said enzyme is a subtilisin-type serine hydrolase and said cysteine is substituted for an amino acid in or near a subsite selected from the group consisting of an S1 subsite, an S1' subsite, and an S2 subsite.
- Sub A1

9. The antagonist of claim 8, wherein said enzyme is a *Bacillus lentus* subtilisin.

10. The antagonist of claim 8, wherein said cysteine is substituted for an amino acid corresponding to a reference residue in a *Bacillus lentus* subtilisin, where said
5 reference residue is at or near a residue selected from the group consisting of residue 156, residue 166, residue 217, residue 222, residue 62, residue 96, residue 104, residue 107, residue 189, and residue 209.

Sub a3
10 11. The antagonist of claim 6, wherein said enzyme is a chymotrypsin-type serine protease and said cysteine is substituted for the amino acid corresponding to a reference residue in a mature trypsin (Protein Data Bank entry 1TPP), wherein said reference residue is at or near a residue selected from the group consisting of Tyr94, Leu99, Gln175, Asp189, Ser190, Gln192, Phe41, Lys60, Tyr151, Ser214, and Lys224.

15 12. The antagonist of claim 7, wherein said enzyme is an alpha/beta type serine hydrolase and said cysteine is substituted for the amino acid corresponding to a reference residue in a *Candida antarctica* lipase (Protein Data Bank entry 1TCA), where the reference residue is at or near a residue selected from the group consisting of Trp104, Leu140, Leu144, Val154, Glu188, Ala 225, Leu278 and Ile285.

13. The antagonist of claim 7, wherein said enzyme is an aspartyl protease.

20 14. The antagonist of claim 13, wherein said enzyme is a pepsin-type protease and said cysteine is substituted for the amino acid corresponding to a reference residue in the mature human pepsin (Protein Data Bank entry 1PSN), where the reference residue is at or near a residue selected from the group consisting of Tyr9, Met12, Glu13, Gly76, Thr77, Phe111, Phe117, Ile128, Ser130, Tyr189, Ile213, Glu239, Met245, Gln287,
25 Met289, Leu291, and Glu294.

Sub a3
15. The antagonist of claim 6, wherein said enzyme is an cysteine
protease.

- Sub B7
16. The antagonist of claim 15, wherein said enzyme is a papain and said cysteine is substituted for the amino acid corresponding to a reference residue in a mature papain (Protein Data Bank entry 1BQI), where the reference residue is at or near a residue selected from the group consisting of Asn18, Ser21, Asn64, Tyr67, Trp69, Gln112, Gln142, Asp158, Trp177, and Phe207.
- Sub B8
17. The antagonist of claim 6, wherein said enzyme is a metalloprotease.
18. The antagonist of claim 17, wherein said enzyme is a metalloprotease and said cysteine is substituted for the amino acid corresponding to a reference residue in the mature human matrix metalloprotease (Protein Data Bank entry 830C), where the reference residue is at or near a residue selected from the group consisting of Leu111, Phe175, Tyr176, Ser182, Leu184, Phe189, Tyr214, Asp231, Lys234, and Ile243.
19. The antagonist of claim 1, wherein said target is a molecule present on the surface of a cell.
20. The antagonist of claim 19, wherein said molecule present on the surface of a cell is a molecule forming a receptor.
21. The antagonist of claim 19, wherein said molecule present on the surface of a cell is a ligand.
22. The antagonist of claim 19, wherein said molecule present on the surface of a cell is a component of a cell wall.
23. The antagonist of claim 19, wherein said molecule present on the surface of a cell is a component of a cell membrane.
24. The antagonist of claim 1, wherein said targeting moiety is selected from the group consisting of a protein, an antigen, a carbohydrate, a nucleic acid, a lipid, a coordination complex, a sugar, a vitamin, a dendrimer, and a crown ether.
25. The antagonist of claim 24, wherein said targeting moiety is a cognate ligand for a receptor or an enzyme.

26. The antagonist of claim 24, wherein said targeting moiety is an inhibitor for a receptor or an enzyme.

27. The antagonist of claim 1, wherein said enzyme is a protease and said targeting moiety is a ligand selected from the group consisting of a carbohydrate, a vitamin
5 or vitamin analog, an enzyme inhibitor, a peptide, a pharmaceutical that is a small organic molecule, and biotin.

28. The antagonist of claim 1, wherein said enzyme is a protease and said targeting moiety is a receptor.

29. The antagonist of claim 27, wherein said enzyme is a subtilisin.

10 30. The antagonist of claim 29, wherein said targeting moiety is an enzyme inhibitor that is a pyrazole.

31. The antagonist of claim 29, wherein said targeting moiety is a biotin.

32. The antagonist of claim 29, wherein said targeting moiety is a ligand that binds a lectin.

15 33. The antagonist of claim 32, wherein said lectin is concanavalin A.

Sub B9 34. The antagonist of claim 33, wherein targeting moiety is a carbohydrate.

35. The antagonist of claim 34, wherein said targeting moiety is -thioethyl D-mannopyranoside.

20 36. The antagonist of claim 33, wherein said targeting moiety specifically binds to a soil and said enzyme degrades a component of said soil.

Sub B10 37. A method of degrading a target molecule, said method comprising contacting said target molecule with a catalytic antagonist comprising a targeting moiety that specifically binds to said target molecule said targeting moiety being attached to an enzyme
25 that degrades said target molecule resulting in the release of said antagonist thereby allowing said antagonist to bind and degrade another target molecule.

38. The method of claim 37, wherein said targeting moiety is joined to said enzyme through the sulfur group on a cysteine.

39. The method of claim 38, wherein said cysteine is a cysteine that is substituted for a native amino acid other than cysteine in said enzyme.

5 40. The method of claim 39, wherein said cysteine is a cysteine that is substituted for a native amino acid other than cysteine in or near a subsite comprising a substrate binding site of said enzyme.

Sub-G3 41. The method of claim 39, wherein said enzyme is an enzyme selected from the group consisting of a protease, an esterase, an amidase, a peptidase, a lactamase, a cellulase, an oxidase, an oxidoreductase, a reductase, a transferase, a hydrolase, an isomerase, a ligase, a lipase, a phospholipase, a phosphatase, a kinase, a sulfatase, a lysozyme, a glycosidase, a glycosyltransferase, a nuclease, an aldolase, a ketolase, a lyase, a cyclase, a reverse transcriptase, a hyaluronidase, an amylase, a cerebrosidase and a chitinase.

42. The method of claim 41, wherein said enzyme is a serine hydrolase.

15 43. The method of claim 42, wherein said enzyme is a subtilisin.

44. The antagonist of claim 39, wherein said cysteine is a cysteine that is substituted for an amino acid forming a substrate binding site.

20 45. The method of claim 44, wherein said enzyme is a subtilisin-type serine hydrolase and said cysteine is substituted for an amino acid in or near a subsite selected from the group consisting of an S1 subsite, an S1' subsite, and an S2 subsite.

46. The method of claim 45, wherein said enzyme is a *Bacillus lentus* subtilisin.

Sub-G6 47. The method of claim 45, wherein said cysteine is substituted for an amino acid corresponding to a reference residue in a *Bacillus lentus* subtilisin, where said reference residue is at or near a residue selected from the group consisting of residue 156, residue 166, residue 217, residue 222, residue 62, residue 96, residue 104, residue 107, residue 189, and residue 209.

48. The method of claim 41, wherein said enzyme is a chymotrypsin-type serine protease and said cysteine is substituted for an amino acid corresponding to a reference residue in a mature trypsin (Protein Data Bank entry 1TPP), wherein said reference residue is at or near a residue selected from the group consisting of Tyr94, Leu99, Gln175, Asp189, Ser190, Gln192, Phe41, Lys60, Tyr151, Ser214, and Lys224.

49. The method of claim 41, wherein said enzyme is an alpha/beta type serine hydrolase and said cysteine is substituted for an amino acid corresponding to a reference residue in a *Candida antartica* lipase (Protein Data Bank entry 1TCA), where the reference residue is at or near a residue selected from the group consisting of Trp104, Leu140, Leu144, Val154, Glu188, Ala 225, Leu278 and Ile285.

50. The method of claim 41, wherein said enzyme is an aspartyl protease.

51. The method of claim 50, wherein said enzyme is a pepsin-type protease and said cysteine is substituted for the amino acid corresponding to a reference residue in the mature human pepsin (Protein Data Bank entry 1PSN), where the reference residue is at or near a residue selected from the group consisting of Tyr9, Met12, Glu13, Gly76, Thr77, Phe111, Phe117, Ile128, Ser130, Tyr189, Ile213, Glu239, Met245, Gln287, Met289, Leu291, and Glu294.

52. The method of claim 41, wherein said enzyme is an cysteine protease.

53. The method of claim 52, wherein said enzyme is a papain and said cysteine is substituted for the amino acid corresponding to a reference residue in a mature papain (Protein Data Bank entry Asn18, Ser21, Asn64, Tyr67, Trp69, Gln112, Gln142, Asp158, Trp177, and Phe207).

54. The method of claim 41, wherein said enzyme is a metalloprotease.

55. The method of claim 54, wherein said enzyme is a metalloprotease and said cysteine is substituted for the amino acid corresponding to a reference residue in the mature human matrix metalloprotease (Protein Data Bank entry 830C), where the reference residue is at or near a residue selected from the group consisting of Leu111, Phe175, Tyr176, Ser182, Leu184, Phe189, Tyr214, Asp231, Lys234, and Ile243.

56. The method of claim 37, wherein said target is a molecule present on the surface of a cell.

57. The method of claim 56, wherein said molecule present on the surface of a cell is a molecule forming a receptor.

5 58. The method of claim 56, wherein said molecule present on the surface of a cell is a ligand.

Sub B14 59. The method of claim 56, wherein said molecule present on the surface of a cell is component of a cell wall.

10 60. The method of claim 56, wherein said molecule present on the surface of a cell is component of a cell membrane.

61. The method of claim 37, wherein said targeting moiety is selected from the group consisting of a protein, an antigen, a carbohydrate, a nucleic acid, a lipid, a coordination complex, a sugar, a vitamin, a dendrimer, and a crown ether.

15 62. The method of claim 61, wherein said targeting moiety is a cognate ligand for a receptor or an enzyme.

63. The method of claim 61, wherein said targeting moiety is an inhibitor for a receptor or an enzyme.

20 64. The method of claim 37, wherein said enzyme is a protease and said targeting moiety is a ligand selected from the group consisting of a carbohydrate, a vitamin or vitamin analog, an enzyme inhibitor, a peptide, a pharmaceutical that is a small organic molecule, and biotin.

Sub 99 65. The antagonist of claim 37, wherein said enzyme is a protease and said targeting moiety is a receptor.

66. The method of claim 64, wherein said enzyme is a subtilisin.

25 67. The method of claim 66, wherein said targeting moiety is an enzyme inhibitor that is a pyrazole.

68. The method of claim 66, wherein said targeting moiety is an biotin.

69. The method of claim 66, wherein said targeting moiety is a ligand that binds a lectin.

70. The method of claim 69, wherein said lectin is concanavalin A.

5 71. The method of claim 70, wherein targeting moiety is a carbohydrate.

Sub B15
~~72. The method of claim 70, wherein said targeting moiety is -thioethyl D-mannopyranoside.~~

73. The method of claim 66, wherein said targeting moiety specifically binds to a soil and said enzyme degrades a component of said soil.

10 74. An enzyme having altered substrate specificity said enzyme comprising a targeting moiety attached to a subsite comprising the substrate binding site of said enzyme.

75. The enzyme of claim 74, wherein said targeting moiety is coupled to said enzyme through to a sulfur of a cysteine in said subsite of said enzyme.

15 76. The enzyme of claim 75, wherein said cysteine is substituted for a native amino acid that is not cysteine in said subsite of said enzyme.

20 77. The enzyme of claim 75, wherein said enzyme is an enzyme selected from the group consisting of a protease, an esterase, an amidase, a peptidase, a lactamase, a cellulase, an oxidase, an oxidoreductase, a reductase, a transferase, a hydrolase, an isomerase, a ligase, a lipase, a phospholipase, a phosphatase, a kinase, a sulfatase, a lysozyme, a glycosidase, a glycosyltransferase, a nuclease, an aldolase, a ketolase, a lyase, a cyclase, a reverse transcriptase, a hyaluronidase, an amylase, a cerebrosidase and a chitinase.

78. The enzyme of claim 77, wherein said enzyme is a serine hydrolase.

79. The enzyme of claim 78, wherein said enzyme is a subtilisin.

25 80. The enzyme of claim 76, wherein said cysteine is a cysteine that is substituted for an amino acid forming a substrate binding site.

81. The enzyme of claim 80, wherein said enzyme is a subtilisin-type serine hydrolase and said cysteine is substituted for an amino acid in or near a subsite selected from the group consisting of an S1 subsite, an S1' subsite, and an S2 subsite.

5 82. The enzyme of claim 81, wherein said enzyme is a *Bacillus lentus* subtilisin.

83. The enzyme of claim 81, wherein said cysteine is substituted for an amino acid corresponding to a reference residue in a *Bacillus lentus* subtilisin, where said reference residue is at or near a residue selected from the group consisting of residue 156, residue 166, residue 217, residue 222, residue 62, residue 96, residue 104, residue 107,
10 residue 189, and residue 209.

84. The enzyme of claim 77, wherein said enzyme is a chymotrypsin-type serine protease and said cysteine is substituted for an amino acid corresponding to a reference residue in a mature trypsin (Protein Data Bank entry 1TPP), wherein said reference residue is at or near a residue selected from the group consisting of Tyr94, Leu99, Gln175,
15 Asp189, Ser190, Gln192, Phe41, Lys60, Tyr151, Ser214, and Lys224.

85. The enzyme of claim 77, wherein said enzyme is an alpha/beta type serine hydrolase and said cysteine is substituted for an amino acid corresponding to a reference residue in a *Candida antartica* lipase (Protein Data Bank entry 1TCA), where the reference residue is at or near a residue selected from the group consisting of Trp104,
20 Leu140, Leu144, Val154, Glu188, Ala 225, Leu278 and Ile285.

86. The enzyme of claim 77, wherein said enzyme is an aspartyl protease.

87. The enzyme of claim 86, wherein said enzyme is a pepsin-type protease and said cysteine is substituted for the amino acid corresponding to a reference residue in the mature human pepsin (Protein Data Bank entry 1PSN), where the reference
25 residue is at or near a residue selected from the group consisting of Tyr9, Met12, Glu13, Gly76, Thr77, Phe111, Phe117, Ile128, Ser130, Tyr189, Ile213, Glu239, Met245, Gln287, Met289, Leu291, and Glu294.

88. The enzyme of claim 77, wherein said enzyme is an cysteine protease.

89. The enzyme of claim 88, wherein said enzyme is a papain and said cysteine is substituted for the amino acid corresponding to a reference residue in a mature papain (Protein Data Bank entry Asn18, Ser21, Asn64, Tyr67, Trp69, Gln112, Gln142, Asp158, Trp177, and Phe207).

5 90. The enzyme of claim 77, wherein said enzyme is a metalloprotease.

91. The enzyme of claim 90, wherein said enzyme is a metalloprotease and said cysteine is substituted for the amino acid corresponding to a reference residue in the mature human matrix metalloprotease (Protein Data Bank entry 830C), where the reference residue is at or near a residue selected from the group consisting of Leu111, Phe175, Tyr176,
10 Ser182, Leu184, Phe189, Tyr214, Asp231, Lys234, and Ile243.

Sub a/o 92. ~~The~~ enzyme of claim 37, wherein said target is a molecule present on the surface of a cell.

93. The enzyme of claim 75, wherein said targeting moiety is selected from the group consisting of a protein, an antigen, a carbohydrate, a nucleic acid, a lipid, a
15 coordination complex, a sugar, a vitamin, a dendrimer, and a crown ether.

94. The enzyme of claim 75, wherein said targeting moiety is a cognate ligand for a receptor or an enzyme.

95. The enzyme of claim 75, wherein said targeting moiety is an inhibitor for a receptor or an enzyme.

20 96. The enzyme of claim 75, wherein said targeting moiety is selected from the group consisting of a growth factor, a cytokine, and a receptor ligand.

97. The enzyme of claim 75, wherein said enzyme is a protease and said targeting moiety is a ligand selected from the group consisting of a carbohydrate, a vitamin or vitamin analog, an enzyme inhibitor, a peptide, a pharmaceutical that is a small organic
25 molecule, and biotin.

98. The enzyme of claim 75, wherein said enzyme is a protease and said targeting moiety is a receptor.

99. The enzyme of claim 97, wherein said enzyme is a subtilisin.

100. The enzyme of claim 99, wherein said targeting moiety is an enzyme inhibitor that is a pyrazole.

101. The enzyme of claim 99, wherein said targeting moiety is an biotin.

5 102. The enzyme of claim 99, wherein said targeting moiety is a ligand that binds a lectin.

103. The enzyme of claim 102, wherein said lectin is concanavalin A.

104. The enzyme of claim 103, wherein targeting moiety is a carbohydrate.

10 105. The enzyme of claim 103, wherein said targeting moiety is -thioethyl D-mannopyranoside.

106. The enzyme of claim 99, wherein said targeting moiety specifically binds to a soil and said enzyme degrades a component of said soil.

15 107. A method of directing the activity of an enzyme to a specific target, said method comprising
providing an enzyme having altered substrate specificity said enzyme comprising a targeting moiety attached to a subsite within the substrate binding region of said enzyme; and

contacting said target with said enzyme, whereby said enzyme specifically binds to said target thereby localizing the activity of said enzyme at said target.

20 108. The method of claim 107, wherein said targeting moiety is coupled to said enzyme through to a sulfur of a cysteine in said subsite of said enzyme.

109. The method of claim 108, wherein said cysteine is substituted for a native amino acid that is not cysteine in said subsite of said enzyme.

25 110. The method of claim 108, wherein said method further comprises substituting an amino acid in said subsite with a cysteine and chemically coupling said targeting moiety to said cysteine.

111. The method of claim 107, wherein said enzyme is an enzyme selected from the group consisting of a protease, an esterase, an amidase, a peptidase, a lactamase, a cellulase, an oxidase, an oxidoreductase, a reductase, a transferase, a hydrolase, an isomerase, a ligase, a lipase, a phospholipase, a phosphatase, a kinase, a sulfatase, a lysozyme, a glycosidase, a glycosyltransferase, a nuclease, an aldolase, a ketolase, a lyase, a cyclase, a reverse transcriptase, a hyaluronidase, an amylase, a cerebrosidase and a chitinase.

112. The method of claim 111, wherein said enzyme is a serine hydrolase.

113. The method of claim 112, wherein said enzyme is a subtilisin.

114. The method of claim 109, wherein said cysteine is a cysteine that is substituted for an amino acid forming a substrate binding site.

115. The method of claim 114, wherein said enzyme is a subtilisin-type serine hydrolase and said cysteine is substituted for an amino acid in or near a subsite selected from the group consisting of an S1 subsite, an S1' subsite, and an S2 subsite.

116. The method of claim 112, wherein said enzyme is a *Bacillus lentus* subtilisin.

117. The method of claim 112, wherein said cysteine is substituted for an amino acid corresponding to a reference residue in a *Bacillus lentus* subtilisin, where said reference residue is at or near a residue selected from the group consisting of residue 156, residue 166, residue 217, residue 222, residue 62, residue 96, residue 104, residue 107, residue 189, and residue 209.

118. The method of claim 111, wherein said enzyme is a chymotrypsin-type serine protease and said cysteine is substituted for the amino acid corresponding to a reference residue in a mature trypsin (Protein Data Bank entry 1TPP), wherein said reference residue is at or near a residue selected from the group consisting of Tyr94, Leu99, Gln175, Asp189, Ser190, Gln192, Phe41, Lys60, Tyr151, Ser214, and Lys224.

119. The method of claim 111, wherein said enzyme is an alpha/beta type serine hydrolase and said cysteine is substituted for the amino acid corresponding to a reference residue in a *Candida antartica* lipase (Protein Data Bank entry 1TCA), where the

reference residue is at or near a residue selected from the group consisting of Trp104, Leu140, Leu144, Val154, Glu188, Ala 225, Leu278 and Ile285.

120. The method of claim 111, wherein said enzyme is an aspartyl protease.

5 121. The method of claim 120, wherein said enzyme is a pepsin-type protease and said cysteine is substituted for the amino acid corresponding to a reference residue in the mature human pepsin (Protein Data Bank entry 1PSN), where the reference residue is at or near a residue selected from the group consisting of Tyr9, Met12, Glu13, Gly76, Thr77, Phe111, Phe117, Ile128, Ser130, Tyr189, Ile213, Glu239, Met245, Gln287,
10 Met289, Leu291, and Glu294.

122. The method of claim 111, wherein said enzyme is an cysteine protease.

123. The method of claim 122, wherein said enzyme is a papain and said cysteine is substituted for the amino acid corresponding to a reference residue in a mature
15 papain (Protein Data Bank entry 1BQI), where the reference residue is at or near a residue selected from the group consisting of Asn18, Ser21, Asn64, Tyr67, Trp69, Gln112, Gln142, Asp158, Trp177, and Phe207.

124. The method of claim 111, wherein said enzyme is a metalloprotease.

125. The method of claim 124, wherein said enzyme is a metalloprotease
20 and said cysteine is substituted for the amino acid corresponding to a reference residue in the mature human matrix metalloprotease (Protein Data Bank entry 830C), where the reference residue is at or near a residue selected from the group consisting of Leu111, Phe175, Tyr176, Ser182, Leu184, Phe189, Tyr214, Asp231, Lys234, and Ile243.

but all
25 ~~126. The method of claim 75, wherein said targeting moiety is selected from the group consisting of a protein, an antigen, a carbohydrate, a nucleic acid, a lipid, a coordination complex, a metal, a sugar, a vitamin, a dendrimer, and a crown ether.~~

127. The method of claim 107, wherein said targeting moiety is a cognate ligand for a receptor or an enzyme.

128. The method of claim 107, wherein said targeting moiety is an inhibitor for a receptor or an enzyme.

129. The method of claim 107, wherein said targeting moiety is selected from the group consisting of a growth factor, and a cytokine.

5 130. The method of claim 107, wherein said enzyme is a protease and said targeting moiety is a ligand selected from the group consisting of a carbohydrate, a vitamin or vitamin analog, an enzyme inhibitor, a peptide, a pharmaceutical that is a small organic molecule, and biotin.

Put a 12 10 131. The antagonist of claim 107, wherein said enzyme is a protease and said targeting moiety is a receptor.

132. The method of claim 130, wherein said enzyme is a subtilisin.

133. The method of claim 132, wherein said targeting moiety is an enzyme inhibitor that is a pyrazole.

134. The method of claim 132, wherein said targeting moiety is an biotin.

15 135. The method of claim 132, wherein said targeting moiety is a ligand that binds a lectin.

136. The method of claim 135, wherein said lectin is concanavalin A.

137. The method of claim 136, wherein targeting moiety is a carbohydrate.

20 138. The method of claim 136, wherein said targeting moiety is -thioethyl D-mannopyranoside.

139. The method of claim 132, wherein said targeting moiety specifically binds to a soil and said enzyme degrades a component of said soil.

25 140. A method of enhancing the activity of a drug that acts as an inhibitor of a receptor or an enzyme, said method comprising:
coupling a serine hydrolase to said drug such that when said drug binds said receptor or enzyme, the serine hydrolase degrades the receptor or enzyme.

141. The method of claim 140, wherein said method increases the dosage therapeutic window of said drug.

142. The method of claim 140, wherein said serine hydrolase is a subtilisin.

143. A method of inhibiting an enzyme or a receptor, said method
5 comprising contacting the enzyme or receptor with a chimeric molecule comprising a ligand that binds said enzyme or receptor attached to an enzyme that degrades the cognate ligand of said enzyme or receptor.

144. The method of claim 143, wherein said chimeric molecule comprises a protease attached to an inhibitor of said enzyme or receptor.

10 145. The method of claim 144, wherein said protease is selected from the group consisting of a serine protease, a cysteine protease, an aspartyl protease, a pepsin-type protease, and a metalloprotease.

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